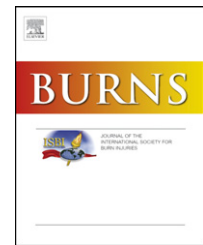


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The efficacy of Aloe vera, tea tree oil and saliva as first aid treatment for partial thickness burn injuries

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ABSTRACT

Many alternative therapies are used as first aid treatment for burns, despite limited evidence supporting their use. In this study, Aloe vera, saliva and a tea tree oil impregnated dressing (Burnaid[®]) were applied as first aid to a porcine deep dermal contact burn, compared to a control of nothing. After burn creation, the treatments were applied for 20 min and the wounds observed at weekly dressing changes for 6 weeks. Results showed that the alternative treatments did significantly decrease subdermal temperature within the skin during the treatment period. However, they did not decrease the microflora or improve re-epithelialisation, scar strength, scar depth or cosmetic appearance of the scar and cannot be recommended for the first aid treatment of partial thickness burns.

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1. Introduction

First aid is emergency care or treatment given before regular medical aid can be obtained. In the case of a burn, it should provide analgesia and ideally halt the progression of injury. A prospective audit of 341 new burn patients who presented to the Stuart Pegg Pediatric Burns Centre at the Brisbane Royal Children's Hospital in 2005 (data not shown) identified a number of alternative treatments applied by the public for the first aid treatment of burns. Although approximately 72% of people did use cold or ice water as first aid for burns, there were still a considerable number who used alternative therapies such as Aloe vera or tea tree oil products. Approximately 13% of patients had a Burnaid[®] dressing (a tea tree oil impregnated hydrogel dressing (sponge) developed by Rye Pharmaceuticals (Roseville, NSW, Australia)) applied as first aid for their burns, either alone or in conjunction with cold water. In most of these cases, the Burnaid[®] was applied

by Queensland Ambulance on route to the hospital. Approximately 2% of patients had Aloe vera applied as first aid for their burns, either alone or in conjunction with cold water.

Although their use is widespread, alternative treatments usually have little evidence to support their use. There is one published study (with no statistical analysis) comparing Burnaid[®] to water cooling in a porcine model [1]. This study found that 15 °C compresses and Burnaid[®] reduced skin temperature and improved re-epithelialisation compared to control, although the 15 °C compresses were slightly better than Burnaid[®]. A recent review of four clinical trials investigating the effect of Aloe vera on burn wounds found that Aloe vera significantly shortened the wound healing time (by approximately eight days) compared to control. They concluded that it may be an effective treatment for first and second degree burns [2]. However, another study examining the effect of Aloe vera on gynecological wounds (wounds complicated by haematomas, seromas or abscess formation

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which were surgically opened or spontaneously underwent dehiscence) [3] found that the gel significantly delayed wound healing by approximately 30 days. Animal studies testing Aloe vera are conflicting, with two studies using guinea pig burns showing that Aloe vera both improved [4] and hindered burn wound healing [5]. Previous studies have shown that saliva has a positive effect on wound healing. Animals lick their wounds instinctively and desalivated rats and mice show a delay in wound healing [6,7]. The application of saliva to skin cells in culture [8] was found to stimulate the metabolic cell activity in a time and dose dependent manner in a comparative, or better manner than 10% foetal calf serum. Extracts from the submandibular and sublingual glands were found to be more effective than parotid gland extracts, indicating the healing effect is specific to salivary components, rather than a generalized moist environment. This effect was confirmed in rat wounds [9] and the application of saliva to bovine wounds was also found to be beneficial [10].

This study examines the efficacy of commonly used alternative first aid treatments (Burnaid[®] dressing, Aloe vera and saliva) on a porcine deep dermal burn injury. As the current recommendations are to cool the burn wound (usually with cold tap water), the cooling ability of these treatments was measured as well as their long-term (6 weeks) effect on wound healing and scar formation.

2. Materials and methods

2.1. Animal surgery

All animal work was approved by the institutional animal ethics committee. Eight Large White juvenile pigs of 25–32 kg (average 29.1 kg, approximately 8 weeks of age) were used for the study. Anaesthesia was induced with an intramuscular dose of 13 mg/kg ketamine hydrochloride (Ketamine 100 mg/mL, Parnell Laboratories, Alexandria, Australia) and 1 mg/kg xylazine (Xylazil 20 mg/mL, Ilium, Troy Laboratories, Sydney, Australia) and was maintained with isoflurane via a size 4 laryngeal mask airway [11]. The hair on the back and flanks was clipped and the skin gently wiped with clean water prior to wounding. Buprenorphine hydrochloride at 0.01 mg/kg (Temgesic 0.3 mg/mL, Reckitt Benckiser, West Ryde, Australia) was administered as an analgesic on induction. The animals were positioned on a flat table, lying on one side with the flank for burn creation upward.

To measure subdermal temperature during burn creation and first aid treatment, a temperature probe was inserted under the skin. A 14-gauge cannula was inserted obliquely beside each wound area and advanced under the dermis until the tip was in the centre of the burn area. The needle was removed from the cannula and a type K thermocouple (Radiospares Components Pty Ltd, Smithfield, Australia) was inserted and taped into position. A digital 54II Fluke thermometer (Fluke Australia Pty Ltd, North Melbourne, Australia) automatically collected and logged temperature measurements every 15 s once the burning device was applied and during the course of the 20 min first aid treatment.

Wounds were created using a technique described previously by our group [12]. A Pyrex laboratory Schott (Mainz,

Germany) Duran[®] 500 mL bottle was used which had the bottom removed and replaced with plastic wrap, which was secured with tape around the base (approximately 8 cm diameter). The bottle was filled with 300 mL of sterile water and heated in a microwave oven until it was 92.0 °C, whereupon the device was placed on the pig flank in a specific anatomical position on the dorsal flank. Immediately prior to burning, a fine mist of room temperature water was sprayed on the wound area to facilitate wound creation. The device was held in place for 15 s. Two burns were created on each animal, one on each flank. As the animal had to be lying flat on each side for the burn to be created (for best contact), the animal had to be flipped horizontally after the first burn had been created before the second one could be produced on the opposite flank.

2.2. Administration of alternative first aid treatment

After the first burn created on the first flank, the treatment was commenced as soon as practically possible (within 10 s, which is a realistic delay for treatment of accidental burns). After this time the animal was also turned over to lie on the other flank. The second burn was then created on the opposite flank and treatment again applied within 10 s. One of the 4 different treatments (Aloe vera, Burnaid[®], saliva, control) was applied for 20 min to each burn, starting from the time of burn creation. Each animal received the same treatment on both wounds. For control animals, after the burn was created, nothing was applied to the skin for 20 min. For the Aloe vera treatment, leaves of a mature, well-established plant were skinned and enough of the inner pulp and gel was collected and applied directly to the wound to cover it. The Burnaid[®] treatment (Rye Pharmaceuticals) (10 cm square dressing) was applied directly to the wound. Saliva was collected from a human volunteer before burn creation and continually applied to the wound over the 20 min treatment period as it dried out. After the 20 min treatment period, the wounds were dressed with Jelonet[™] (inert paraffin gauze, Smith & Nephew, Hull, UK) and Melolin[™] (Smith & Nephew, Hull, UK) secured with Fixomull[®] retention tape (BSN Medical, Hamburg, Germany). The Aloe vera and saliva were left on the wound under the dressings. The Burnaid[®] dressing was removed, but the gel residue also remained on the wound under the dressing. The animals were then put into custom-made garments to protect the dressings and wounds over the 6-week period.

2.3. Microbiology

To obtain a semi-quantitative examination of the microflora present with each treatment, the clipped porcine flank was swabbed prior to wound creation, after wound creation and after the treatment application of 20 min. The wounds were also swabbed 2 weeks later, when the wounds typically are exuding and colonisation may be present. Swabs which were pre-moistened in saline were taken of each wound for 16 wounds, 2 wounds in each treatment. As the burn areas were well defined, a standard area was swabbed within the burn margin to ensure comparable microbial assessment. Transport media was used to minimise loss of organisms in transit.

Table 1 – The cosmetic parameters examined in photographs taken at week 6 after burn by three experienced burn observers

Scar colour	Scar height	Amount of hair	Scar border contraction	Final appearance
0—Normal	0—Normal	0—Normal over all	0—Normal, smooth oval	0—Excellent
1—Normal centre with scar ring	1—Slightly raised 1 mm	1—Normal over some	1—Some border irregularity	1—Minor scar
2—Pink	2—Moderately raised 2 mm	2—Only a few hairs	2—Most of border contracted	2—Moderate scar
3—Red	3—Very much raised >2 mm	3—No hair	3—Severely contracted edges	3—Severe scar
4—Purple				
5—Dark purple				

A higher score indicates a worse cosmetic outcome.

Swabs were cultured on the same day of collection and were evenly spread over the surface of a Horse Blood agar plate, MacConkey Agar plate, Colistin Naladixic Acid Agar plate and Sabouraud Agar plate. A 16-streak plate technique was used to spread the inoculum. All media was incubated at 35 °C in a non-CO₂ incubator for a total of 48 h. Cultures were examined at both 24 and 48 h. The degree of growth of each bacterial isolate was recorded as scant, 1–3+ in accordance with the streak pattern. Organisms were identified to the genus level using standard laboratory techniques (Gram stain, catalase, oxidase).

2.4. Dressings and sedation

For weekly dressing changes, the animals were sedated with an intramuscular dose of ketamine/xylazine (13 mg/kg ketamine/1 mg/kg xylazine). The wounds were examined and a clinical description of the wound was noted, observing characteristics such as re-epithelialisation, scar profile and presence of hair. Photographs were taken of the wound using a Canon EOS 400D digital SLR camera (Canon Australia Pty Ltd, North Ryde, Australia). The perimeters of the wounds were traced using a Visitrak™ device (Smith & Nephew, Hull, UK) which calculates the total area of the wound in cm². Results were expressed as mean ± standard error of the mean from the replicates for each treatment group.

The animals were euthanized at 6 weeks after the burn with 15 mL of sodium pentobarbitone (Lethabarb 325 mg/mL, Virbac (Australia) Pty Ltd, Peakhurst, Australia). Representative tissue biopsies approximately 1 cm³ were collected from the burn (four biopsies) and the unburned normal areas (two biopsies) and fixed in 10% formalin for paraffin embedding.

2.5. Histology: light microscopy

Paraffin sections of 4 µm thickness were stained with haematoxylin and eosin (H&E) and digital images captured under a Nikon EP600 microscope fitted with a Spot RT slider cooled CCD camera (Nikon Australia Pty Ltd, Lidcombe, Australia). The thickness of the skin sections (epidermis, dermis) and the amount of organising granulation tissue was measured digitally from the images using Image Pro Plus v4.1.29 software (Media Cybernetics Inc, Silver Spring, USA) in a blinded fashion.

2.6. Clinical assessment

The photographs of the wounds at post mortem (6 weeks after burn) were examined in a blinded fashion at a later date by three burn observers (a burn surgeon, a burn nurse and a burn scientist, all with experience examining burn wound healing in animal models) and graded using a point scale. The parameters examined are outlined in Table 1. For each characteristic, the higher the score, the worse the wound/scar outcome. Each individual observer graded each wound on each characteristic.

2.7. Statistical analysis

The statistical analysis of this study was conducted with Minitab® R14 (Minitab Inc., Chicago, 2003). The level of significance of every individual test was set at 5% ($p < 0.05$) and the actual p -values were additionally derived. The degree of agreement between the three assessors was analysed with the Fleiss' kappa test. The average clinical scores of the three assessors and the histology results were analysed with univariate and multivariate ANCOVAs with non-homogeneous slopes in the treatment groups where the covariate was the percentage of redness of an individual wound at creation. In the statistical analyses, the averages for each pig (not wound averages) were used to determine significant differences between treatment groups. All results are expressed as mean ± standard error of the mean from the replicates for each treatment group.

3. Results

3.1. Wound creation

The wounds at creation all had white eschar with a hyperaemic circle around the wound border. Some small areas of the wounds had a red erythematous appearance. From previous studies these areas are known to be more superficial in depth and heal faster than the other white areas. In order to standardize the wounds, the red area was measured and expressed as a % of the total wound area for each burn and later used as a covariate in statistical analysis. There was no significant difference in the % red of wounds between any of the groups and the average red area for the wounds in this study was $10.8 \pm 1.8\%$. The order that the

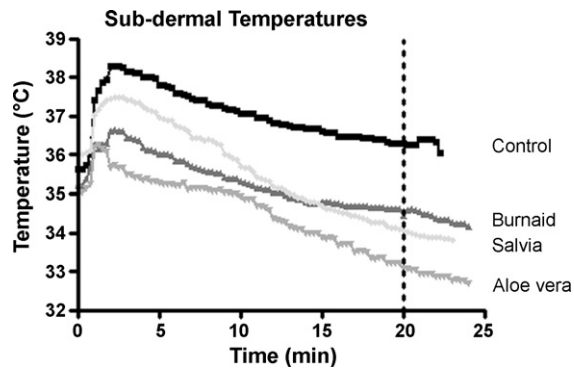


Fig. 1 – The subdermal temperatures during the 20 min treatment period. The dotted line indicates the end of the 20 min treatment period. At 5 min, the Aloe vera treated skin was significantly colder than control ($p = 0.03$). At 20 min, both the Aloe vera and saliva treated skin were significantly colder than the control ($p = 0.02$ and 0.05 , respectively). The S.E.M.s were 0.73°C at 5 min and 1.15°C at 20 min.

wounds were created in on each animal also did not significantly alter the wound outcome or the % red of the wounds.

3.2. Skin and rectal temperatures

The subdermal temperatures were recorded every 15 s during the 20 min treatment period for each wound. Fig. 1 shows the average temperature for each treatment group. All treatments

had some cooling effect compared to the control. After 5 min of treatment, the wounds treated with Aloe vera were significantly colder than the control ($p = 0.03$). After the 20 min treatment period, both Aloe vera and saliva were significantly colder than the control at the subdermal level ($p = 0.02$ and 0.05 , respectively).

Skin surface temperatures on the burn and surrounding skin were measured during the burn, immediately after treatment had commenced and at the end of the 20 min treatment period. Interestingly, when the burns were being created, the surrounding normal skin dropped in temperature by approximately 1.7°C . By the end of the treatment period, the temperature of the control burns had dropped by 8.7°C compared to the temperature immediately after creation. The skin temperature measurements of the treated burned skin were highly variable because of the evaporative cooling effect of the different treatments. However, it was noted that when an air current was passed over the Burnaid® dressing for approximately 20–30 s, the skin temperature dropped by 3.5°C almost immediately and remained low, demonstrating the dressing's powerful evaporative cooling ability.

Rectal temperatures dropped by approximately 0.6°C over the 20 min treatment period and were irrespective of treatment.

3.3. Re-epithelialisation

The re-epithelialisation was measured and recorded at each week during the dressing change (Fig. 2A and B). There were no significant differences between the treatments and control, however there was a trend for the wounds in the saliva group

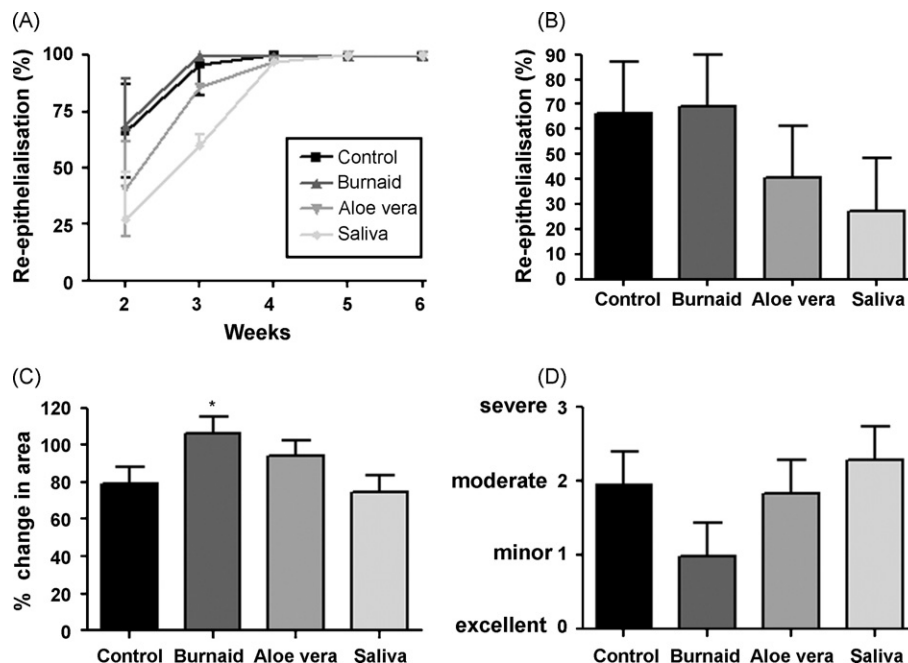


Fig. 2 – Re-epithelialisation of the wounds from weeks 2–6 (A) or at week 2 (B). There were no significant differences between the treatments and control. The area of scar at week 6 after burn was expressed as a % of the initial burn area (C). The Burnaid® scars were significantly larger than the control scars ($p = 0.02$) and were slightly larger than the initial wound area (average = 107%). The cosmetic final appearance of the scar (D). There were no significant differences between any of the treatments and control, however, there was a trend for the Burnaid® treatment to have a slightly better cosmetic outcome than the control and other treatments, although this was not significant.

to heal more slowly than the control wounds at weeks 2 and 3 ($p = 0.08$).

3.4. Skin histology

Paraffin sections of burn and normal skin were stained with haematoxylin and eosin and were analysed using Image Pro Plus software to measure the thickness of epidermis, thickness of dermis and the amount of organising granulation tissue (OGT) [12]. There were no significant differences between any of the treatments and the control for any histological parameter.

3.5. Wound area

The area of scar present at week 6 after burn was measured and expressed as a % of the initial burn area (Fig. 2C). The Burnaid® scars were significantly larger than the control scars ($p = 0.02$) and some were in fact larger than the initial wound area (scar area average = $107 \pm 9.0\%$).

3.6. Cosmetic appearance

Photographs of the wounds were scored at week 6 by three experienced burn observers and rated for the parameters: scar colour, scar height, amount of hair, scar border contraction and final cosmetic appearance. The degree of agreement between the observers was assessed with the Fleiss' kappa and found to be statistically acceptable for each attribute except amount of hair. The overall percentage of agreement for wounds was 62.5, 62.5, 37.5, 56.25 and 56.25% for the final appearance, border contraction, amount of hair, scar height

and scar colour respectively. Ideally the coefficient of agreement between observers should be above 80%. In this study the assessor's scores for each wound did not differ by more than one point on each scale, however the average agreement between observers was 55%. In future work, the assessment panel will be further trained so there is greater concurrence and the scales may be modified to reduce variability. The results were similar for all parameters, so only the final appearance graph is shown (Fig. 2D). There were no significant differences between any of the treatments and control, however, there was a trend for the Burnaid® treatment to have a slightly better cosmetic outcome than the control and other treatments, although this was not significant. This may be related to the increase in scar size caused by the dressing, which may make the scars look less contracted, and slightly more cosmetically appealing.

3.7. Microbiology

Swabs at all time points showed mixed growth of: *Staphylococcus* species, non-haemolytic *Streptococcus*, yeast and lactose fermenting Gram negative rod (Table 2). These organisms are typical of what would be expected on the skin surface of normal healthy animals. Interestingly, although burns are considered sterile due to the heat applied to the skin during creation, swabs taken immediately after burn creation showed the presence of many isolates. The Burnaid® treatment appears to slightly inhibit *Staphylococcus* species and yeast. Also worth noting is that the saliva treated wounds showed similar isolates to the control wounds, indicating that the poor results obtained with saliva were apparently not due to bacterial load.

Table 2 – The microflora present for each treatment

	Skin	Burn	Treatment	2 Weeks later
Control	Staph sp3+ Non-haem Strep 3+ Non-lactose fermenting Gram –ve 3+ Yeast 2+ <i>Aspergillus niger</i> sc (1 cfu)	Staph sp3+ Non-haem Strep 3+ Non-lactose fermenting Gram –ve 2+ Yeast 2+ <i>Aspergillus niger</i> sc (3 cfu)	Staph sp. 3+ Non-haem Strep 3+ Yeast 2+ <i>Aspergillus niger</i> sc (3 cfu) <i>Aspergillus terreus</i> sc (1 cfu)	Staph sp. x2 3+ Non-haem Strep 3+ Lactose fermenting Gram –ve rod 2+
Burnaid	Staph sp. 3+ Non-lactose fermenting Gram –ve 2+ Non-haem Strep 3+ Yeast 2+ <i>Bacillus</i> sp. 2+	Staph sp. 2+ Non-haem Strep 3+ Yeast 1+	Staph sp. 2+	Staph spx2 3+ Non-lactose fermenting Gram –ve rod x2 2+
Aloe vera	Staph sp. x2 3+ Non-haem Strep 2+ Yeast 3+ <i>Aspergillus niger</i> (1 colony)	Staph sp. 3+	Staph sp. 3+ Non-haem Strep 1+	Staph sp. 3+ Non-haem Strep 3+ <i>Pseudomonas aeruginosa</i> 3+
Saliva	Staph sp. x2 3+ Non-haem Strep 3+ Yeast 2+	Staph sp. x2 2+ Non-haem Strep 2+ Yeast 2+	Staph sp. 3+ Non-haem Strep 3+ Yeast 1+ Alpha-haem Strep 3+	Staph sp. 3+ Non-haem Strep 3+ Lactose fermenting Gram –ve rod 3+

Swabs were taken of the porcine skin prior to burn, after the burn was created, after the 20 min treatment period and 2 weeks later at the dressing change. The number of colonies which resulted were scored on a four point system. Abbreviations: (sp.) species, (cfu) colony-forming unit, (–ve) negative, (Staph) *Staphylococcus*, (Strep) *Streptococcus*, (Non-haem Strep) Non-haemolytic *Streptococcus*.

During the dressing period, some of the wounds became colonised and odiferous. Two of these wounds were in the control group and three in the saliva group. This difference between control/saliva and Aloe vera/Burnaid[®] treatment was significant ($p = 0.02$, likelihood ratio test), indicating that Aloe vera and Burnaid[®] may have had antimicrobial properties that decreased the chance of burn wound colonisation.

4. Discussion

This study tested the effects of alternative treatments Aloe vera, Burnaid[®] and saliva on a porcine partial thickness burn injury. The parameters measured were; speed of re-epithelialisation, histology and strength of the scar and cosmetic appearance. It is worth noting that these treatments were only tested as first aid treatments, with an application time of 20 min, and it may be that prolonged application of these treatments during the re-epithelialisation process may help wound healing. All of these agents are also believed to have soothing or analgesic properties, however this could not be measured in this study. As burns are painful, analgesic properties of any treatment should not be underestimated, however a good burn first aid treatment should both soothe and lessen the damage caused by the burn.

Initially for the saliva treatment it was envisaged that the animal's own saliva would be used on its wounds. However, it proved impossible to collect enough saliva for this purpose. Because human saliva was used instead of autologous saliva, this may have contributed to the poor results obtained with this treatment. It may be that animal's own saliva confers more benefit than another species or that the human volunteer's saliva contained something inhibitory. However, the microbiology analysis showed that saliva did not contain more bacterial isolates than control, so bacterial contamination is unlikely to be the reason for poor growth promotion.

There were several different measures of temperature recorded in this first aid study. It was interesting to observe that the surrounding skin temperature decreased suddenly when the burn was being created—this may reflect localized vasoconstriction occurring as a result of thermal damage. This will be further investigated using a laser Doppler in the future. All treatments displayed a capacity for evaporative cooling, which is probably the origin of their analgesic properties. In particular, Burnaid[®] was able to decrease the skin surface temperature by several degrees within less than a minute. Obviously this also raises the concern of the dressing's ability to cause hypothermia. Several patients with large body surface area burns who have presented to the adult burn unit in Brisbane after Burnaid[®] dressing application and transport have been reported to be in a hypothermic state (personal communication, Dr. Michael Rudd, Royal Brisbane and Women's Hospital Burn Unit).

This study found that the first aid application of Aloe vera, Burnaid[®] or saliva proved to be no better than a control of nothing in terms of re-epithelialisation, histology of the scar or cosmetic appearance. It was also found that while Aloe vera and saliva reduced the subdermal temperature, they did not improve the wound outcome compared to control. This evidence suggests that there are non-thermal mechanisms

responsible for progressive tissue destruction and that perhaps cooling is not the only mechanism by which first aid can be effective. Although cooling has been recommended for the first aid treatment of burn injuries since the time of Galen (AD129–199) (predominantly for the relief of pain), there is still some debate over whether colder water is more beneficial than water at room temperature or just below skin temperature (e.g. 22–25 °C) for improving the healing of burn injuries. Many animal studies show that compared to nothing, cooling improves the speed of burn wound healing [1,13,14] and decreases the size of the scar [15], however these studies do not compare different temperatures of water. The studies that do compare different temperatures of water focused on mortality rates [16] or capillary leakage/edema [17], rather than wound healing. The study of the wound healing ability of warmer water compared to cold water and the examination of possible non-thermal benefits of first aid (e.g. reduction in locally circulating inflammatory cytokines/enzymes) are the subject of ongoing work.

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Conflict of interest

There are no conflicts of interest for any of the authors.

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